REMARKS

Claims 10-14, and 17-20 are pending in the present patent application. Claims 13 and 14 are allowable per the Official Action dated 19 March 2001; Applicants thank the Examiner for allowing these claims.

Applicants have cancelled claims 10 and 17 herein without prejudice to later prosecute the subject matter of this claim.

Applicants have amended claim 12 to recite "SEQ ID Nos: 1,2 ,and 3" in part c, and have deleted part (h) of claim 12. No new matter is added by this amendment.

Rejection Under 35 USC, Section 112, Second Paragraph

Claim 12 has been rejected under 35 USC, Section 112, Second Paragraph as indefinite for the recitation of "SEQ ID NO:4" in part (c) of claim 12, and further for the recitation of a "complementary nucleic acid molecule" in part (h).

In response, Applicants have amended claim 12, item (c) to recite "fragments of SEQ ID Nos: 1, 2, and 3;", and Applicants have deleted part (h) of claim 12.

In view of the amendments to claim 12, Applicants respectfully request reconsideration and removal of the rejection under 35 USC, Section 112, Second Paragraph.

Rejection Under 35 USC, Section 112, First Paragraph

Claim 10 has been rejected under 35 USC, Section 112, First Paragraph as allegedly not enabled by Applicants' specification. Applicants have canceled claim 10 herein, thereby rendering this rejection now moot.

Claims 11, 12, 18, and 19-20 have been rejected under 35 USC, Section 112, First Paragraph as allegedly containing subject matter that was not in Applicants' possession at the time the application was filed. According to the Examiner, the use of the terms "allelic variant" and "splice variant" in these claims are not properly supported in Applicants' specification. The Examiner asserts that "Alleles may result in altered mRNAs or polypeptides ***whose structure or function may or may not be altered...***These definitions [of splice variants and allelic variants in Applicants' specification] do not provide any specific information about the structure of

naturally occurring (alleles) variants or splice variants of SEQ ID NOS: 4, 5, [or] 6 nor discloses [sic] any function for naturally occurring variants".

In response, Applicants assert that the terms "allelic variant" and "splice variant" as used by Applicants are fully supported by Applicants' specification for the following reasons. Claims 11 and 12 encompass only ***biologically active beta-secretase polypeptides***. Production of beta-secretase polypeptides, fragments, variants and the like is set forth on pages 21 *et seq.* of Applicants' specification. Thus, the skilled artisan could easily prepare a very large number of candidate beta-secretase polypeptides by simply following the guidance provided by Applicants in the specification. Applicants' specification clearly defines a "biologically active beta-secretase polypeptide" on page 14, lines 18-27. This definition provides that such polypeptide or fragments thereof would be capable of cleaving the APP Swedish mutation peptide EVKMDAEF between the methionine and aspartic acid residues. On pages 114-119 of Applicants' specification, a detailed description of such cleavage assay is provided. Thus, the skilled artisan could readily, using only routine procedures, run any number of potential beta-secretase candidate polypeptides and fragments through this assay, and clearly identify those beta secretase molecules having such peptide cleaving ability. Such molecules, and only such molecules, would fall within the scope of claims 11 and 12 and all claims depending therefrom as biologically active beta secretase polypeptides. Thus, without detailed information as to the structure, amino acid sequence, "tolerance" for amino acid substitution, or the like, the skilled artisan could quickly and accurately determine which molecules are encompassed by claims 11, 12, and 18-20. Thus, contrary to the Examiner's statement above, *all splice variants and allelic variants encompassed by Applicants' invention have a well defined functional activity*, and, the claims are fully enabled by Applicants' specification.

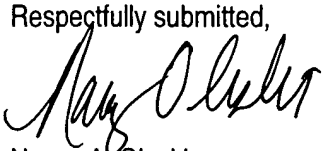
In view of the foregoing, Applicants respectfully request reconsideration and removal of the rejection under 35 USC, Section 112, First Paragraph.

Rejection Under 35 USC Sections 102/103

Claims 10 and 17 have been rejected under 35 USC, Section 102(a) as anticipated by, or alternatively under 35 USC, Section 103(a) as obvious over, Chrysler et al (WO 96/40885). These claims have been canceled herein, thereby rendering this rejection now moot.

Applicants believe that the claims as set forth herein are in condition for allowance, and a notice to that effect is respectfully solicited.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

12. (Twice Amended). An isolated biologically active polypeptide encoded by a nucleic acid molecule selected from the group consisting of:

a) the nucleic acid molecule as set forth in any of SEQ ID NOs: 1, 2, and 3;

b) a nucleic acid molecule encoding the polypeptide of any of SEQ ID NOs: 4, 5, and 6;

c) fragments of SEQ ID [NO: 4] NOs: 1, 2, and 3;

d) an allelic variant or splice variant of any of (a) or (b);

e) a nucleic acid molecule of the DNA vector insert in ATCC Deposit No. 207158;

f) a nucleic acid molecule of the DNA vector insert in ATCC Deposit No. 207159; and

g) a nucleic acid molecule encoding a polypeptide having one to fifty conservative amino acid substitutions as compared with the polypeptide of SEQ ID NO: 4. [; and

h) a nucleic acid molecule that is the complement of any of (a)-(g) above.]